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CHEMICAL & ENGINEERING NEWS

C&EN

MAY 16, 1994

CHEMICAL COMPANY EARNINGS RISE SUBSTANTIALLY IN FIRST QUARTER PAGE 30

Fine & Intermediate Chemicals

Producers respond to environmental, market pressures

Page 10

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CHEMICAL & ENGINEERING NEWS
C&EN
MAY 16, 1994

NEWS OF THE WEEK

■ If a promising new Merck drug to treat AIDS proves out, work by the company to develop a low-cost, high-yield process may be crucial for commercialization. **Page 6**

■ NSF awards nine U.S. cities $15 million each to improve science, math, and technology education programs for inner-city children. **Page 7**

■ Arco announces plan to raise up to $1 billion by offering debt securities linked to stock in Lyondell Petrochemical, opening path to possible divestiture of the Houston-based company. **Page 7**

■ In a move to advance the links between computer science and biotechnology drug design, two major computer industry executives make a substantial investment in a startup drug-development firm. **Page 8**

■ U.S. and U.K. researchers announce construction of a reversible "molecular switch" that is triggered by either pH change or electrochemical oxidation-reduction, based on a molecular "bead" encircling a "thread." **Page 8**

■ Initiatives to advance development of science and technology in Africa are discussed at a forum in Washington, D.C. **Page 9**

COVER: Workers at AlliedSignal Performance Chemicals, Morristown, N.J., produce oxime intermediates to special order

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BUSINESS

First-quarter results are good news for major chemical companies—solid sales contributed to strong earnings and production rose, as did profitability. **Page 30**

Restructuring is theme of Chemical Management & Resources Association meeting, and reaction to the topic is as varied as the way the term is defined. **Page 34**

Unilever is introducing a "new generation" concentrated detergent to European markets—one with a formulation unusual enough to spawn two legal actions in the Netherlands. **Page 35**

GOVERNMENT

House passes NSF reauthorization bill—one of many bills being considered by Congress—that allows for 4.2% growth in 1995 and 2.6% growth in 1996; the measure goes to the Senate next. **Page 38**

Agricultural chemical makers note that Congress is beginning to consider usefulness of risk assessment in setting regulatory priorities and formulating regulations on the use of chemicals. **Page 40**

SCIENCE/TECHNOLOGY

Stanford University chemists have created a random library of single amino acid mutants of myoglobin to discover new ligand binding pathways in the protein. **Page 49**

Handheld electronic chemical calculator currently under development could change the way that chemistry is taught and become an accessory to research. **Page 50**

NEWS FOCUS

Producers of fine and intermediate chemicals face major changes in their markets, sparked by the increasing emphasis on chiral drugs and tougher environmental regulations. Page 10

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LETTERS

A human chain reaction

Last fall, I attended the annual retirees reunion of Dow Corning. It was a special year being the 50th anniversary of Dow Corning. Seated next to me was Frank Hyde, the chemist who made Dow Corning possible. It was a special year for him, too, his 90th birthday anniversary. The conversation led to our experiences at Harvard University and the powerful impact Harvard had on organic chemistry in the U.S. Frank's commentary helped sharpen my memory of stories about Harvard that I had heard years before from another Frank—F. C. Whitmore—when I was one of his last graduate students at Penn State.

Whitmore likened his experience at Harvard to being part of a "human chain reaction." He was one of a small group of chemistry students who, in today's sports parlance, I would name the "Fabulous Four." The other three were Roger Adams, Henry C. Gilman, and James B. Conant. They were not all in exactly the same graduating class, but as both undergraduate students at Harvard and as graduate students in organic chemistry their student careers had considerable overlap. One of their most influential teachers, Elmer P. Kohler, initiated the chain reaction. He instilled in all four the love of teaching. He constantly drew on their unusual talents to get them to teach each other. When necessary, he deflated their not inconsiderable egos by asking probing questions that none could answer. Probably at no other time in the history of chemistry teaching did four such talented students fill the halls of learning of a single school at the same time. The chain reaction gathered strength.

In those years just after the turn of the century, it was de rigueur for chemistry students to go to Germany for doctoral studies. The combination of a satisfactory undergraduate experience at Harvard and the looming prospect and then the reality of the First World War kept all four away from Germany and at school in the U.S.

In 1905, Adams was the first of the four to start at Harvard as an undergraduate and to receive a Ph.D. degree (1912). In 1916, he went to the University of Illinois and became head of the department of chemistry there in 1926. Under his marvelous tutelage, there was a great outpouring of well-trained organic chemists from Illinois, most of whom would play important roles as industrial chemists.

The youngest of the four was Gilman, who received a B.S. degree from Harvard in 1915 and a Ph.D. degree in 1918. He, too, became a professor of chemistry—at Iowa State. In my day, it was a requirement of graduate students to own the twin green books by Gilman. He would become a good personal friend of mine since we both shared a love of organosilicon chemistry. He was the most long-lived of the four, with a life of over 90 years, which he devoted to research and teaching. Being a "Gilman student" was a term of highest accolade. Gilman was the first recipient of the American Chemical Society's Frederic Stanley Kipping Award in Organosilicon Chemistry, sponsored by Dow Corning Corp., for excellence in organosilicon research. He had a fond and friendly rivalry with Whitmore in this research arena during the 1940s. Whitmore was very anxious to publish a communication in the *Journal of the American Chemical Society* of my first research on *tert*-butyltrichlorosilane "before Henry scoops us."

Conant was the "Harvard Man of the Century." He received an A.B. degree in 1913, a Ph.D. degree in 1916, and stayed on. I feel as if I knew him personally because my love of organic chemistry was first nurtured when we used his most excellent textbook for study at the University of Scranton in 1939. Conant's legendary prowess as an educator was continually evident. He became a full professor, and then in 1933, went on to be a renowned member of that elite group—Harvard presidents. In 1948, his name was floated quite seriously as a possible candidate for the U.S. Presidency. And he is one of the few chemists whose face has graced the cover of *Time* magazine.

Correction

• May 2, page 9: A business concentrate on Shanghai Petrochemical misstated the company's sales and earnings. Sales increased 43% to $872 million in 1993, not $871,560. Earnings rose 90% to $100 million, not $100,000.

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Market, Environmental Pressures Spur Change In Fine Chemicals Industry

Increasing emphasis on chiral drugs, more stringent environmental rules are among economic and technical issues confronting producers

Stephen C. Stinson,
C&EN Northeast News Bureau

Makers of fine chemicals have much in common with other parts of the chemical industry. Although ways of doing business may be somewhat different, the major concerns—including markets, new product development, process economics, environmental stewardship, and attention to core technologies—are the same.

For the fine chemicals industry, these issues were ratcheted to a new level of intensity at ChemSpec Europe '94, the international meeting of fine chemicals producers held last month in Manchester, England. Indeed, developments surfacing in Manchester create a picture of an industry not only responding to change but generating it as well.

From a business standpoint, for example, the fortunes of the fine chemicals industry are especially sensitive to changes in the pharmaceutical industry, which consumes about half the fine chemicals industry's output. One development about to make its mark is the growing emphasis on chiral drugs. Single enantiomers of chiral drugs have long been a focus of medicinal chemists and process engineers, but observers in Manchester told C&EN that significant orders for compounds have at last begun to arrive.

Environmental matters, too, affect the industry. Fine chemicals producers worldwide naturally must accommodate their own governments' increasingly stringent environmental regulations. But in some of those countries, environmental regulations are still less exacting than those of the U.S. In their own self-interest, firms outside the U.S. realize that most of their customers are nevertheless in the U.S., and American customers hesitate to appear linked to suppliers who might have environmental problems.

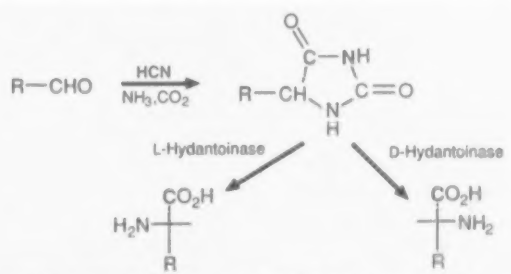
Technologically, the fine chemicals industry is a substantial market for firms that supply intermediates, catalysts, and equipment. Such goods help producers cut production steps and costs, as well as decrease the number of waste streams to be treated. At the same time, fine chemicals producers are constantly expanding and deepening the particular chemistries at which they excel.

Analyst Enrico T. Polastro of Arthur D. Little International, Brussels, estimates the value of worldwide fine chemicals sales in the range of $26 billion to $34 billion. This includes bulk active ingredients as well as intermediates for end uses such as drugs and pesticides. Drugs alone take $15 billion to $17 billion worth, Polastro says, perhaps a 50 to 60% share.

Within the drug market, dollar sales for single enantiomers of chiral drugs are likely to grow at the expense of racemates, says analyst Ray Ceriotti of Technology Catalysts International Corp.,

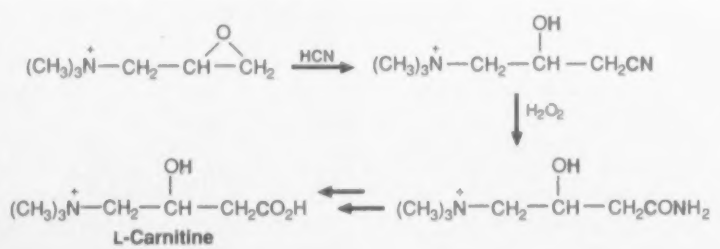
Hydrogen cyanide is core technology for amino acids

Hydantoins yield enantiomeric amino acids . . .

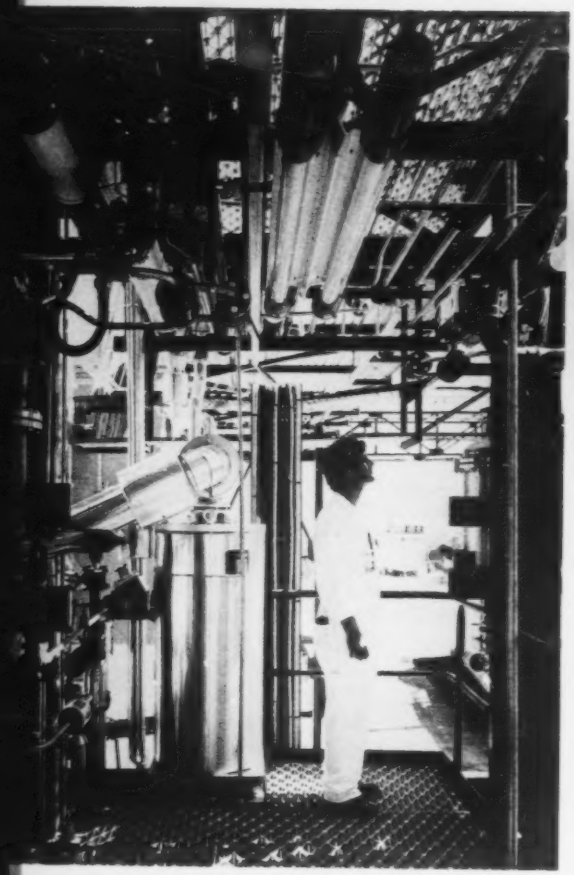


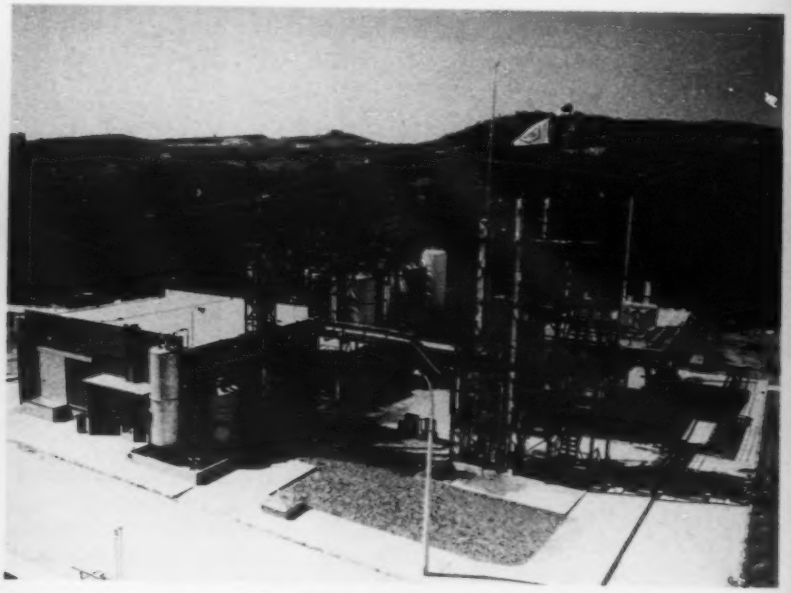
R = $C_6H_5CH_2$—, $(CH_3)_2CH$—, $CH_3CH_2CH_2$—, $CH_3CH_2CH_2CH_2$—, $(CH_3)_2CHCH_2$—, $C_6H_5CH_2CH_2$—, CH_3SCH_2—, or CH_3—

. . . and an epoxide opening gives carnitine



Source: Degussa





Drug producer Hovione reduced solvent use and built a solvent and raw material recovery unit (above) in Loures, Portugal, that won an environmental prize from the European Union. Plant operator (left) monitors methanol recovery columns.

Falls Church, Va. Also, sales of enantiomeric drugs will grow faster than sales of fine chemicals generally, he adds, because of the greater added value in production.

In light of the heavy weighting toward drugs, Polastro predicts thoroughgoing changes in the worldwide fine chemicals industry over the next 15 years. Polastro sees three alternative courses of events unfolding as health care reform proceeds in many countries, and he assigns a probability to the development of each over time.

He labels these alternatives "business-as-usual," "cost cutting," and "rational." He rejects the business-as-usual alternative out of hand, assigning the present state of affairs only a 20% chance of persisting to 1995 and vanishing completely by 1997.

By cost cutting, Polastro means the employment of drastic measures to contain costs, with companies and institutions the targets. Although marked by rigid government control, this course of action would involve only incremental impact and extent of health care reforms. Rather, this narrow, rigid, price-based policy would put the burden mainly on drugs, creating demand for the cheapest available ones without regard to cost-benefit analyses.

Any cost-cutting phase would hit fine chemical makers severely. Because drug companies would be searching for all possible ways to cut production expenses, their fine chemicals suppliers would feel some of the pain.

But the cost-cutting policy would change neither patients' and institutions' drug-buying procedures essentially nor the current structure of drug companies and distributors, or hospital, chain, and neighborhood pharmacies. Some governments—and here Polastro thinks of Spain—may set up their own generic drug factories. Polastro sees the cost-cutting scenario as likeliest in the short term, with a 50% probability of being in place in 1995, rising to 75% by 1997.

In the long term, Polastro is more optimistic and predicts evolution toward a "rational" system. Such a system would be based on cost-benefit relationships, he thinks, rather than just on price. Adoption of the rational course would mean liberalization on the part of government agencies, but it would also bring a profound restructuring of the health care system as suppliers move to adapt to and compete in such a system. Drug companies and their fine chemicals suppliers would benefit as they develop products in this climate. Polastro sees the probability of the rational approach rising slowly and uniformly year by year to 100% by 2010 as reliance on cost cutting recedes toward zero.

Exploiting core technologies

At the Manchester meeting, several fine chemicals firms showed off their core technologies. These are specific chemistries that companies concentrate on in addition to their abilities to draw on all of chemistry where needed for multistep syntheses. Speakers from some companies described those firms' core technologies at the symposium, while other companies introduced new products based on their core technologies at the exposition.

For example, group leader John F. McGarrity at Lonza's research center in Visp, Switzerland, described the company's expertise in hydrogen cyanide and its derivatives, ketene and diketene (4-methyleneoxetan-2-one), and pyridines. He emphasized competitiveness through exploitation of an existing raw materials base and cross-fertilization among different projects.

McGarrity also spoke of the need for "carrier projects" as a means of devel-

Hoechst, Lonza, and Plater Chemicals booths at ChemSpec Europe '94 meeting of fine chemicals producers in Manchester.

oping new core technologies. Carrier projects are those that generate a solid cash product at once, and from which profits pay for deepening the company's experience in that technology thereafter.

In one project, Lonza uses its raw materials position in cyanogen chloride, Cl—C≡N, to make a compound known as Vince's lactam (2-azabicyclo[2.2.1]hept-5-en-2-one). Named for medicinal chemist Robert Vince, who developed it in 1978 while at the University of Minnesota's College of Pharmacy, Minneapolis, the lactam has found use to make carbocyclic ribose drug analogs, most notably in recent years by Chiroscience of Cambridge, England. Indeed, Ray McCague of Chiroscience has described making the lactam by Diels-Alder reaction of *p*-toluenesulfonyl cyanide and cyclopentadiene, followed by hydrolysis.

McGarrity says that methanesulfonyl cyanide is safer to handle, however, and Lonza used that compound to devise a cyclic process to make Vince's lactam on a 100-kg scale. Methanesulfonyl cyanide comes from reaction of sodium methanesulfinate [$CH_3S(O)O^-Na^+$] with cyanogen chloride. Hydrolysis of the Diels-Alder product with cyclopentadiene regenerates methanesulfinate, which is recycled to react with more cyanogen chloride.

Examples of Lonza carrier projects are the company's use of methyl or ethyl δ-chloroacetoacetates to make 2-aminothiazoles and biotin. 2-Aminothiazoles are added as side chains to advanced cephalosporin antibiotic nuclei. Biotin is a feed additive. Profits from sales of these compounds are fueling development of other projects based on four-carbon intermediates and on the proprietary diastereoselective hydrogenation catalyst used to make (+)-biotin.

Regarding cross-fertilization, the idea for the biotin hydrogenation came from an analogous hydrogenation to make the antibiotic thienamycin. As McGarrity put it, "The important message here is that from one project has evolved not only a familiarity with a particular class of intermediates, but also one pivotal building block that provides access to a variety of other product classes. In a more general context, the greater the variety of chemical and technical problems tackled and solved within Lonza, the greater will be the reservoir of expertise available to solve the problems posed by new projects."

Chemist Rudolf Vanheertum of Degussa's subsidiary in Antwerp, Belgium, described that firm's use of hydrogen cyanide and cyanogen chloride as core technologies. Degussa's worldwide hydrogen cyanide capacity is 100,000 metric tons per year, made by platinum-catalyzed reaction of methane and ammonia. Chlorination of hydrogen cyanide yields cyanogen chloride. Vanheertum explains that "because transportation of both compounds is practically prohibited by restrictive regulations, Degussa has concentrated on the synthesis and custom manufacturing of fine chemicals in several multipurpose plants."

From hydrogen cyanide itself come cyanohydrins, amino acids, and amines. For example, reaction with benzaldehyde catalyzed by either (*R*)- or (*S*)-oxynitrilase enzyme produces the cyanohydrins (*R*)- or (*S*)-mandelonitrile of high enantiomeric purity.

Also, reaction of hydrogen cyanide with aldehydes together with ammonia gives α-aminonitriles, which can be hydrolyzed to racemic α-amino acids. Alternatively, hydrogen cyanide, ammonia, and carbon dioxide convert aldehydes to hydantoins (4-alkylimidazolidine-2,5-diones), which can be hydrolyzed with D- or L-hydantoinases to yield D- or L-α-amino acids. And opening of the epoxide of glycidyltrimethylammonium chloride by hydrogen cyanide is a step on the way to the amino acid feed additive L-carnitine [(3-carboxy-2-hydroxypropyl)trimethylammonium hydroxide].

As for production of amines, reaction of isophorone (3,5,5-trimethylcyclohex-2-enone) with hydrogen cyanide is a step on the way to isophoronediamine (5-amino-1-aminomethyl-1,3,3-trimethylcyclohexane), which is useful by itself as an epoxy curing agent or can be converted with phosgene to isophorone diisocyanate, a component of light-stable polyurethane coatings. And reaction of hydrogen cyanide with the 2,4,4-trimethyl-1-pentene isomer of diisobutylene is a route to *tert*-octylamine (2-amino-2,4,4-trimethylpentane), which

is useful because of the *tert*-alkyl group attached to nitrogen.

Elsewhere in Degussa, chiral amino acids are a core technology apart from their production from hydrogen cyanide. Chemist Matthias Kottenhahn of the company's site in Hanau, Germany, says that Degussa produces and markets amino acid enantiomers through its subsidiary, Rexim, in Courbevoie, France, which Kottenhahn says is the largest amino acid producer in Europe.

In addition to L-amino acids that occur naturally in proteins, Rexim makes D-amino acids and nonproteinogenic ones. For example, leucine dehydrogenase catalyzes transformation of trimethylpyruvic acid to nonnatural L-*tert*-leucine (α-amino-β,β-dimethylalanine), which is a component of an experimental Hoffmann-La Roche agent against atherosclerosis. The reduction occurs at the expense of oxidation of cofactor nicotinamide adenine dinucleotide (NADH) to NAD^+. The reduced cofactor is regenerated in a parallel oxidation of ammonium formate to carbon dioxide by formate dehydrogenase.

D-Amino acids give peptides containing them resistance to hydrolysis, Kottenhahn says. Thus D-valine is a component of the pyrethroid insecticide fluvalinate, and D-alanine is part of the artificial sweetener alitame. And a polymethacrylate resin with its pendant carboxyl groups amidized by terminal amino groups of D-lysine is an additive that aids enantiomeric resolution by inhibiting crystallization of one enantiomer from aqueous solutions.

Ozonolysis is a core technology at Chemie Linz, according to Bernt D. Schober. Schober, manager of new business development in custom manufacture, says the Austrian firm has an ozone capacity of 150 kg per hour from two electric discharge generators.

The ozonolysis method is attractive because there are low emissions to the environment, little wastewater, and no residues from the oxidizing agent. The method is also safe because Chemie Linz follows ozonolysis with reduction before workup, so no hazardous compounds accumulate.

Chemie Linz uses its ozone to make glyoxylic acid and derivatives from dimethyl maleate. Schober notes that the Emery Group of Henkel Corp., Cincinnati, has produced azelaic and pelargonic acids from ozonolysis of oleic acid for almost 40 years.

The fragrance compound piperonal [(3,4-methylenedioxy)benzaldehyde] comes from ozonolysis of naturally occurring isosafrole [1,2-(methylenedioxy)-4-propenylbenzene]. And one step in the synthesis of the cephalosporin antibiotic cefaclor is ozonolysis of the exocyclic double bond of a methylenethiazine derivative to the enol of the ketothiazine.

Schober suggests Chemie Linz may show future interest in the synthesis of difunctional compounds as dialdehydes from cyclic olefins, including β-pinene, and 2,5-dihydrofurans, -thiophenes, and -phospholes. The interest in these starting materials is that two functional groups are obtained per mole of ozone.

Nitration and nitric acid oxidation is the core technology at Nobel Chemicals, Karlskoga, Sweden, described by Boris Holm. Holm, who is manager of market development and sales, says the challenge is not only the nitration or oxidation itself but also that nitro or nitrate ester products may be explosive.

Such compounds are dangerous, of course, and also transportation to the customer may be complicated by regulations. So if the purpose of the nitro group is as a functional group handle on the route to another nonnitro compound, Holm says, customers could do well to let Nobel carry out further steps and take delivery of that more advanced intermediate.

Nitric acid oxidation of nitrotoluenes to nitrobenzoic acids yields products of purity needed for drug manufacture, Holm says. The *o*-nitrobenzoic acid is tricky, however, because of the danger of forming explosive picric acid.

Nitrobenzaldehydes are intermediates in production of drugs called calcium channel blockers, which are used for treatment of high blood pressure

Enantiomeric drugs are growing at the expense of racemates

Drug category	Sales, $ billions[a]				% average annual change
	1993	1994	1995	1996	
Achiral	$ 8.4	$ 9.5	$ 9.8	$10.2	7.0%
Racemic	3.9	3.0	2.2	1.4	-29.5
Enantiomeric	22.1	23.0	24.8	26.7	6.6
TOTAL	$34.4	$35.5	$36.8	$38.3	3.7%
ENANTIOMERIC, %	64.3%	64.8%	67.4%	69.7%	

a Data are worldwide sales of final dosage forms for 25 top-selling prescription drugs. **Source:** Technology Catalysts International Corp.

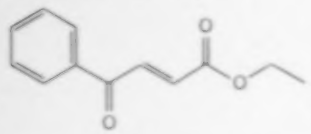
Drug firms have different fine chemicals needs and sourcing strategies

Type of drug firm and examples	Sourcing strategy	Product needs	Product slate
Innovative R&D based (Glaxo, Merck, Hoffmann-La Roche)	Combine in-house production with outsourcing on a case-by-case basis	Customer specific	Broad and related to specific drugs; can include active drugs and intermediates
Branded, multisource (Warner-Lambert, Sterling Winthrop, Zyma)	Rely on merchant market (most drug compounds are freely available and in-house production is rarely cost competitive)	Industry specific	Narrow (for example, in over-the-counter products, only 20 to 30 compounds are used); focus is on active drugs, not intermediates
Generic producers (Lyphomed, Apothecon, Abbott Hospital Products)	Rely on merchant market (keeps capital investment lean; backward integration would reduce flexibility to shift product line)	Industry specific	Broad (more than 400 drugs are available as generic formulations); focus is on active drugs, not intermediates

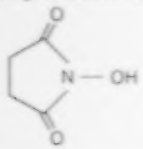
Source: Arthur D. Little International

Fine Chemicals:
New in Pilot Quantities

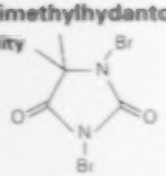
Ethyl benzoyl acrylate



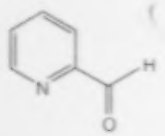
N-Hydroxy succinimide



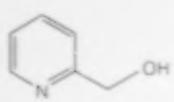
Dibromo dimethylhydantoin
Pharma Quality



Pyridine-2-aldehyde



2-Hydroxy methyl pyridine



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CIRCLE 57 ON READER SERVICE CARD

Chiroscience and Eastman booths at Manchester meeting.

and congestive heart failure. So from *o*-nitrobenzaldehyde come the nifedipine and nisoldipine discovered by Bayer. *m*-Nitrobenzaldehyde gives nicardipine (Yamanouchi) and nimodipine and nitrendipine (both Bayer).

Another important intermediate at Nobel is *p*-nitrobenzoic acid, Holm says, used to make the anesthetic procaine, the vitamin folic acid, and *p*-aminobenzoic acid (PAB). PAB is a feed additive, especially for fish farming, and its esters are sunscreens. The *N*-*p*-aminophenylamide of PAB is under study as a replacement for carcinogenic benzidine in dyes. And the diester of PAB with 1,3-propanediol may replace possibly carcinogenic methylenebis(*o*-chloroaniline) (MOCA) as a polyurethane cross-linking agent, if government agencies ban MOCA.

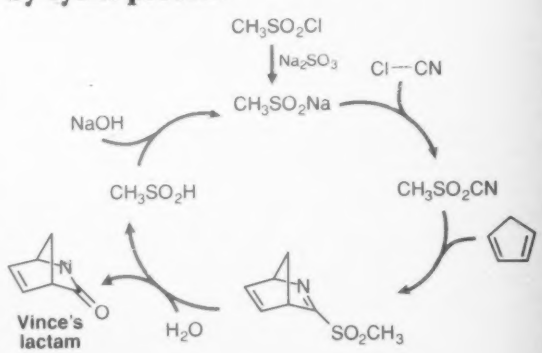
Another new development at Nobel is production of several aminochlorobenzoic acids. The interest there is that Nobel has found an inhibited hydrogenation catalyst from Degussa that reduces nitro groups to amino groups without expelling chlorine from the molecule.

New products launched

Nitration, oxidation, and reduction are also strengths of Ems Dottikon, Dottikon, Switzerland. At the exposition, the company unveiled monosubstituted piperazines, substituted *o*-phenylenediamines, indoles, indazoles, and benzimidazoles as new products based on these. For example, the company makes 1-acetyl-, cyclohexylmethyl-, and ethylpiperazines free of disubstituted compounds. Also new are 4-chloro- and 5-methoxyindole, as well as indolecarboxylic acids and esters. By way of reassuring customers about attention to the environment, Ems Dottikon will start up a new waste incinerator this summer.

Cyclopropanes make up the core technologies at Hüls of Marl, Germany. Some of these compounds come from condensations of ethylene dihalides with malonate esters, which can be followed by hydrolysis and decarboxylation. The company's other cyclopropanations are proprietary. The new products from Hüls include 2-methyl-, 2,2-dimethyl-, and unsubstituted cyclopropanecarboxylic acids and esters,

Versatile intermediate is made by cyclic process



Source: Lonza

and carbonamides, carbonitriles, carboxaldehydes, carbinols, and carbinyl chlorides.

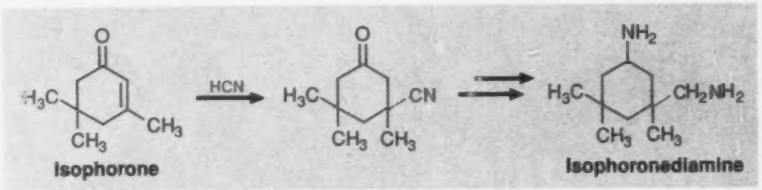
Sepracor of Marlborough, Mass., has prospered on enantioselective technologies licensed from academic chemists. In Manchester, the company showed off an enantioselective method of its own.

Sepracor has previously licensed the asymmetric dihydroxylation of olefins invented by organic chemistry professor K. Barry Sharpless of Scripps Research Institute, La Jolla, Calif., and the asymmetric epoxidation of olefins invented by organic chemistry professor Eric N. Jacobsen of Harvard University. Tradenamed ChiRedox-AR, the new technique uses a catalyst with a proprietary enantiomeric ligand to mediate reduction of carbonyl groups and olefins with diborane.

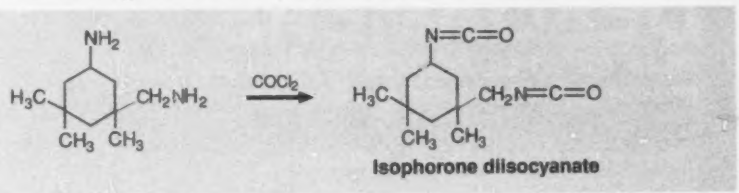
The technique reduces alkyl phenyl ketones to enantiomeric carbinols, *N*-isopropylphenylglyoxaldimine to either enantiomer of 2-dimethylamino-1-phenylethanol, ethyl α-methylcinnamate to ethyl β-phenylbutyrates, and β-acetaminocinnamic acid to *N*-acetylphenylalanines. Sepracor is offering a half-dozen new enantiomeric intermediates based on the reduction.

Celgene Corp. of Warren, N.J., exhibited commercially viable direct enzymatic conversion of racemic nitriles to enantiomeric carboxylic acids by nitrilases without having to go through intermediate amides. Previously, workers had to use a nitrile hydratase and

Hydrogen cyanide is a route to an epoxy resin hardener . . .



. . . or an ingredient of polyurethane coatings



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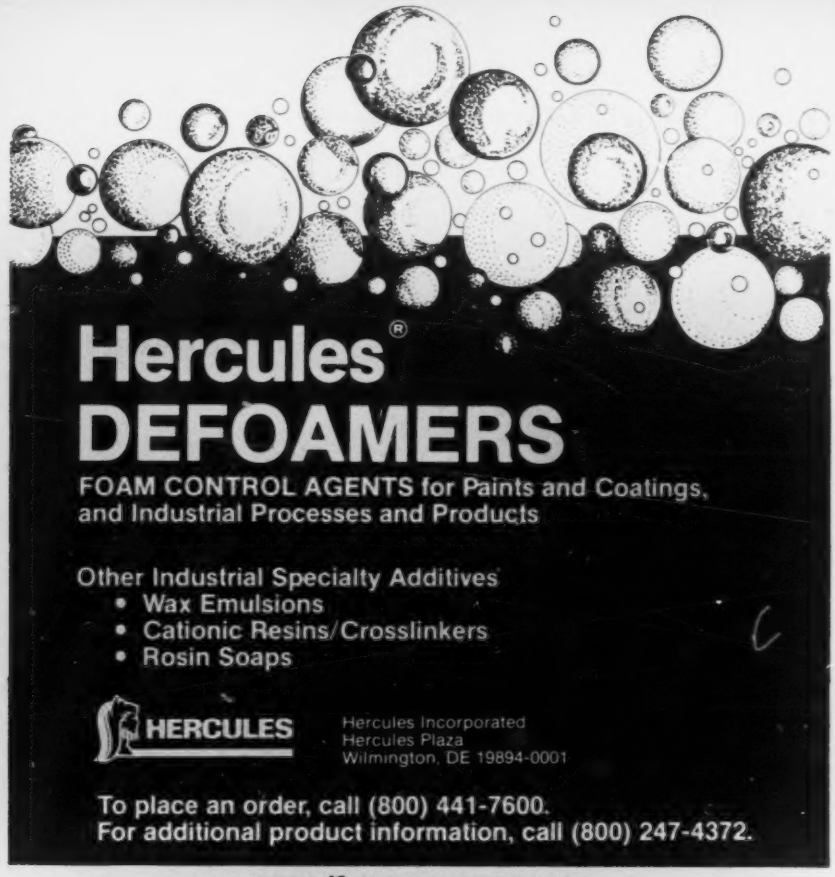

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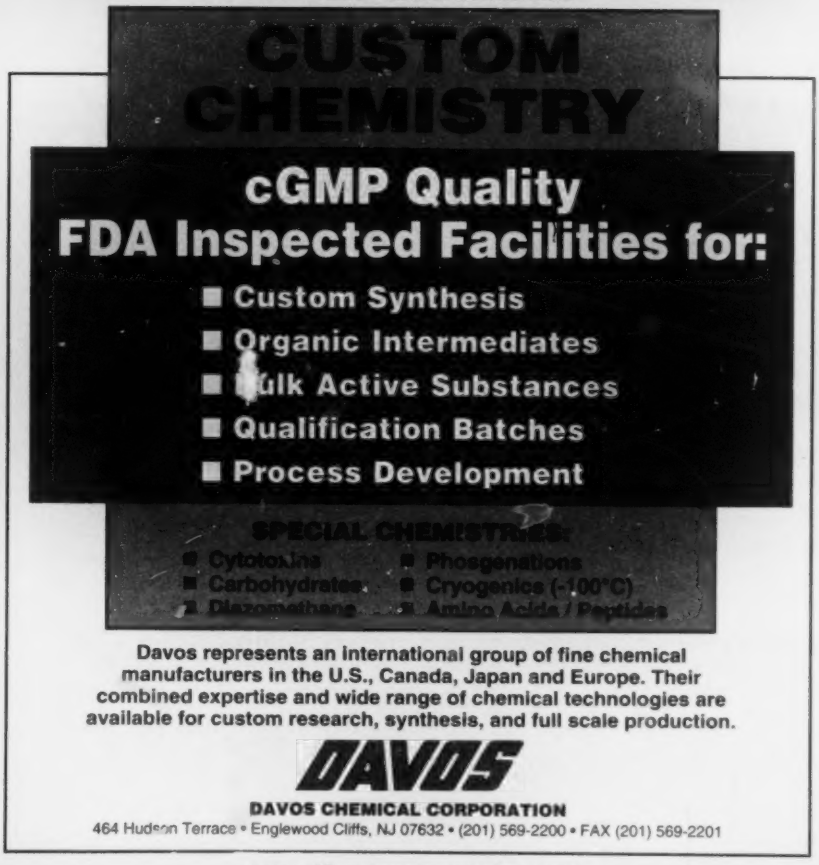
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Conferences, expositions bring producers, buyers

In addition to this year's ChemSpec Europe, three annual conventions are held in the U.S. to bring together sellers and prospective buyers of fine chemicals. Chemical Specialities USA '94 will meet in Chicago, Oct. 18–20, for its fifth year. Also, the 10th Annual Informex Trade Show & Technical Symposium will be held in Nashville, Feb. 20–22, 1995. And although enantiomers of chiral compounds are only a subset of fine chemicals, Chiral USA '94, held earlier this month in Reston, Va., was the second U.S. meeting of a yearly symposium dealing with their production and marketing.

Informex is sponsored by the Synthetic Organic Chemical Manufacturers Association (SOCMA) and focuses on custom chemical production. Most exhibitors also have catalogs of standard intermediates, however. Next year's meeting features a technical session, for which the program is not yet fixed, and a two-day exposition. That meeting is expected to draw 200 exhibitor firms and 1,400 attendees. For information, contact SOCMA, 1330 Connecticut Ave., N.W., Washington, D.C. 20036; phone (202) 659-0060.

Both the Chiral USA and Chemical Specialities USA conferences are organized by Spring Innovations, Stockport, England. For information about either event, in North America contact Brandon Associates, P.O. Box 1244, Merrimack, N.H. 03054, phone (603) 424-2035. Chiral USA '95 will be held at the Boston Marriott Long Wharf, May 14–16, 1995.

Chemical Specialities USA '94, which includes two days of technical sessions and an exposition with more than 100 firms exhibiting, is organized by FMJ International Publications, Redhill, England.

In addition, ChemSpec Europe '95 will take place in Essen, Germany, June 20–22.

an amidase in sequence to get this overall transformation.

Celgene spokesmen see the method as a route to alkyl-, aryl-, amino-, halo-, and hydroxy acids. In particular, the company is hoping it will be a low-cost route to such "profen" (α-substituted propionic acid) analgesics as ibuprofen, flurbiprofen, and ketoprofen. The race-

mic propionitrile could be converted to the desired enantiomeric profen, and the unreacted nitrile racemized and the racemate sent back through the nitrilase step.

At its booth, NutraSweet introduced chiral auxiliary reagents based on its position in L-phenylalanine, a component of the company's synthetic sweetener, aspartame. Chiral auxiliaries are enantiomeric compounds attached covalently to substrate compounds during multistep syntheses. The auxiliaries induce asymmetry into the substrate molecules and are cleaved off when no longer needed.

The new auxiliary compounds are (*S*)-enantiomers of 4-benzyl-2-oxazolidinone and its *N*-acetyl derivative, and 2-methyl-4-phenyloxazoline. The company will market these compounds through its fine chemicals subsidiary, NSC Technologies, also located in Mt. Prospect, Ill. And because D-phenylalanine is available as well, NSC also expects to offer the (*R*)-enantiomers of these auxiliaries soon.

Chiroscience of Cambridge, England, was also in Manchester to offer additions to its own line of enantiomeric synthons (advanced intermediates with broad applications). The company, which recently changed its name from Chiros, is in the businesses of supplying enantiomeric intermediates, redeveloping existing racemic drugs in enantiomeric forms ("racemic switches"), and discovering its own new enantiomeric drugs.

The intermediates shown at ChemSpec include single isomers of Vince's lactam, *tert*-leucine, *endo*-5-norbornen-2-ol, 2-alkoxycyclohexanones, piperidine-2-carboxylic acid, *cis*-3-cyclopentene-1,2-diol, 3-butyn-2-ol, 3-buten-2-ol, and the *N*-*tert*-butoxycarbonyl-protected derivative of 3-(4-thiazolyl)alanine. Chiroscience sees Vince's lactam, which it also lists as "γ-lactam," as an opening to all-carbocyclic antiviral analogs of nucleosides. Peptides containing *tert*-leucine gain metabolic hydrolytic resistance. And the butenol and butynol are useful for making alkaloids, steroids, vitamins E and K, and hormonelike messenger substances called prostaglandins.

Business development managers for FMC Corp.'s Lithium Division, Gastonia, N.C., came to Manchester to offer what they call applications-based synthesis. By this they mean application of the company's expertise in organolithium chemistry to carry out certain reactions or sequences of reactions to special order. The product furnished to the customer may not be an organolithium but rather may be based on a precursor that is.

Chemetall of Frankfurt, Germany, introduced lithium diisopropylamide (LDA) and lithium bis(trimethylsilyl)-amide. These are potent bases used in organic syntheses, such as the production of enolates, which have the virtue of being nonnucleophilic. They are furnished as 10% solutions in hexane, and the LDA solution contains a proprietary stabilizer.

Managers from Callery Chemical Co., Pittsburgh, Pa., came to Manchester to announce the coming onstream of their new diborane plant in Evans City, Pa. The plant has a capacity of 60,000 lb per year of diborane, 110,000 lb per year of dimethylamine-borane complex, and 180,000 lb per year of pyridine-borane. Callery makes diborane beginning with

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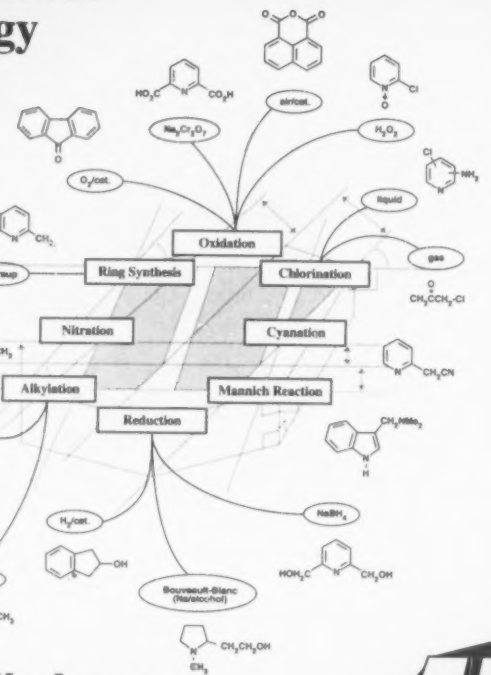

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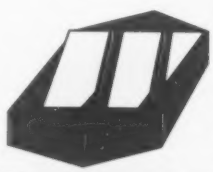

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CIRCLE **9** ON READER SERVICE CARD

conversion of borax to trimethyl borate. That ester reacts with sodium hydride to form sodium borohydride. And sodium borohydride yields diborane on treatment with boron trifluoride.

Eastman Chemical Co. mounted a display from the company's Liverpool, England, location. Eastman maintains a catalog of about 100 stock items but adds and deletes compounds every year. New this year are 10 substituted phenylmalondialdehydes, 10 heterocyclic arylmalondialdehydes, 10 aryl-β-keto esters, 20 methyl phenyl sulfones, and 10 indoles, including the 1-hydroxy-6-methanesulfonyl derivative.

Weyl of Mannheim, Germany, a subsidiary of Rütgerswerke, introduced fluorenylidene-4,4-diphenol, whose diglycidyl ether shows promise in epoxy resins. The fluorene nucleus renders such resins hydrophobic, which is valuable in tropical climates where epoxy adhesives, coatings, and potting compounds can degrade from humidity.

Environmental concerns

Environmental protection was the concern expressed in several presentations in Manchester. For example, heterogeneous catalysts were described that can be filtered away from reaction mixtures and reused, so they don't end up in a waste stream for treatment. And enzymes or cell cultures usually work without leaving a heavy-metal residue.

A literally prize-winning approach has been that of drug producer Hovione, headquartered in Lisbon, Portugal. Fiona Macleod, chief of process engineering at the company's plant in nearby Loures, described the measures that led the European Community, now called the European Union, to award the firm its Better Environment for Industry Prize for 1992.

The company produces about 60,000 kg of semisynthetic tetracycline antibiotics and 200 kg of corticosteroids per year. Important materials used include solvents acetone and methanol and triphenylphosphine-rhodium hydrogenation catalyst.

Hovione did not win the award by coming from behind. "The question of environmental protection has always been addressed at Hovione," Macleod says, "and Hovione's waste stream has always been subject to control and treatment. But most of our customers are in the U.S., so it was obvious that we had to exceed local legislation."

Association goes to bat for specialty chemical makers

The British Association for Chemical Specialities (BACS), organizer of the ChemSpec Europe symposia, is the advocate for British specialty chemical producers, representing them both to British and European Union legislative and regulatory bodies. BACS's 135 member firms are concerned mostly with such formulated specialty chemicals as industrial biocides, specialty surfactants, and water-borne polymers. Despite this variety, the most successful ChemSpec Europe symposia programs have focused increasingly on the fine chemicals segment of specialty chemicals.

For 10 years, Alan W. B. Cowan has been director of BACS. Cowan will step down as director this year but will stay on as secretary. BACS has selected consultant Richard J. Farn as the new director.

Farn says he will move BACS headquarters offices from Sutton, near London, to Manchester or a location close by. He explains that Manchester is the center of gravity of the British specialty chemicals industry.

By improving their processes, Hovione engineers were able to reduce solvent use 20 to 30%. Building a separate, $5 million dedicated recovery and treatment plant further improved efficiency of solvent use so that purchase of new solvents was reduced by 85% overall. Macleod explains that the recovery-treatment plant was purposely built physically apart and functions administratively as a stand-alone entity so that engineers could run it independently and not just as an adjunct to production.

Solvent recovery became economically more favorable when the U.S. Food & Drug Administration accepted the company's specifications for recycled solvents. For example, the recovered acetone contains a small amount of water, but water is added to acetone before use in the processes anyway. And the methanol is slightly alkaline, but methanol is acidified before use in processes.

Rhodium is recovered as a concentrate and sent to Degussa for reclamation and a credit. Originally, managers

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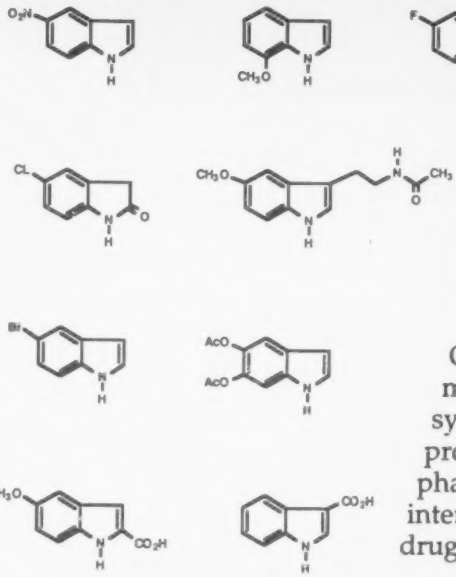

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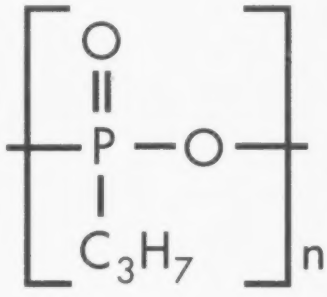

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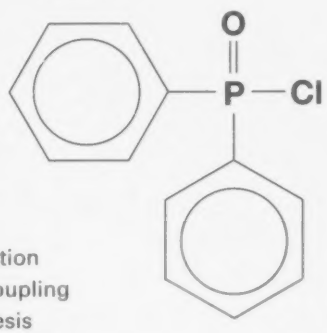

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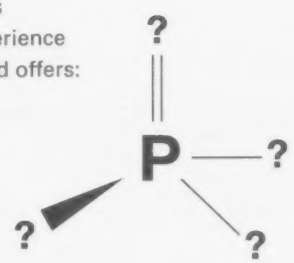

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at Hovione looked to then-high prices of rhodium to defray many expenses. But rhodium prices have since tumbled, and it is the economics of solvent recovery that make the whole operation viable.

"Rich" solvent streams (high-solvent/low-water content) are targeted for distillation and recovery. "Lean" streams go for incineration, with cogeneration of steam. One aqueous stream from acetone recovery must pass through the incinerator because base-catalyzed condensation of acetone produces trace amounts of diacetone alcohol and mesityl oxide, which render the water "too smelly" for sending to the local sewage works.

Macleod describes the only loose end as triphenylphosphine, which ends up as the oxide. The company so far has been unsuccessful in selling the oxide and lacks the capability to recover triphenylphosphine. Macleod says that Hovione welcomes suggestions about what to do with the triphenylphosphine oxide.

As to use of heterogeneous catalysts to design environmentally acceptable processes, Brian Trenbirth, technical director of Contract Chemicals, Knowsley, England, described his firm's line of "supported reagents" at the Manchester meeting. Tradenamed Envirocats, these are proprietary preparations based on impregnation of clay or alumina with chemicals. They are used in catalytic amounts to mediate benzoylations, acetylations, alkylations, arenesulfonylations, and air oxidations.

Advantages of the catalyst intended to replace anhydrous aluminum chloride in benzoylations and acetylations are many. For example, it is used in 10% of the usual amount of aluminum chloride, can be filtered off afterward, often can be reused, is inert to water, does not leave residue in products, is not a chemical irritant, and does not cause scrambling of such groups as methyl. Nor does it cause disproportionations, in which products rearrange intermolecularly to give a mixture of polymethylated and unmethylated molecules.

The catalyst's insensitivity to water is demonstrated by reaction conditions for processes involving benzene. The user adds the catalyst to the benzene in the reactor and simply distills until the azeotrope has carried off all the water from the "wet" benzene. In those cases where

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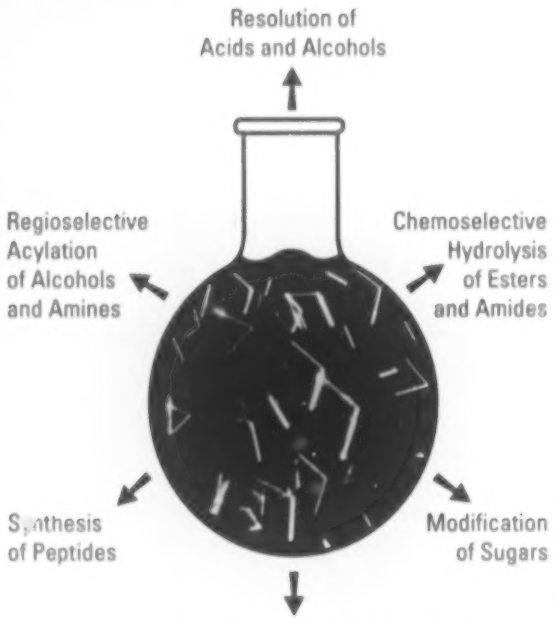

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the catalyst cannot be reused, Contract Chemicals will take it back, still damp with solvent, for regeneration.

Catalysts are available for benzoylation with benzoyl chloride; acylation with acid chlorides or anhydrides; benzylation with benzyl or benzal chloride; alkylation with alkyl halides, olefins, or formaldehyde (production of diarylmethanes); arenesulfonations with arenesulfonyl chlorides; and such air oxidations as that of *o*- or *p*-ethylaniline to aminoacetophenones.

Zeolites also serve as heterogeneous catalysts in making fine chemicals, according to Andreas Vogt of CU Chemie Uetikon, Lahr, Germany. Vogt, who is manager of product development, notes that these aluminosilicate catalysts make possible many useful transformations without the toxic or corrosive compounds often required.

For example, a titanium zeolite catalyzes formation of cyclohexanone oxime from cyclohexanone, ammonia, and hydrogen peroxide. Thus there is no need to use hydroxylamine. And a zeolite called Y catalyzes the Beckmann rearrangement of cyclohexanone oxime to caprolactam, the precursor of nylon 6, without need for strong mineral acids.

In another rearrangement, *m*-phenylenediamine is converted to a mixture of 2-amino-6-methyl- and 4-amino-2-methylpyridines. And a zeolite catalyzes the Fries rearrangement of phenyl acetate or benzoate to a mixture of *o*- and *p*-hydroxyacetophenones and -benzophenones, bypassing the problems of using anhydrous aluminum chloride as catalyst.

The titanium zeolite finds use in Italy to produce 10 million kg per year of catechol and hydroquinone from phenol and hydrogen peroxide, Vogt says. And the mordenite form of zeolite catalyzes nitration of benzene without use of sulfuric acid.

Process safety concerns

In addition to the environment, process safety is a constant concern in the fine chemicals industry. The fear is that a process may be inherently unstable, which means that at a certain temperature, a reaction may become autocatalytic and run away.

Process engineers have long known that they must add reactants to a vessel at a rate so that the temperature does not rise too much too fast. But slow rates of dosing large reactors lead to longer reaction times that hurt the economics of production and allow time for side reactions and product decomposition to occur.

As Jimmy B. Hunter of SynProTec, Manchester, England, points out, the volume of a reactor—the amount to be cooled—increases as a cubic function of the dimensions. But the surface area available to apply cooling increases only as the square. Hunter cites the case of a British company that divides batches of 2,4-dichlorophenol production among six reactors in order to add chlorine fast enough to keep batch times under 15 hours.

Hunter is commercial director at SynProTec, a chemical engineering consulting firm. The firm specializes in designing loop reactors to a client's order for chemical reactions. A loop reactor system continuously circulates the reaction mixture out of the reaction vessel through heaters, coolers, and mixers as needed to keep the reaction under control.

Loop reactors are well known. Indeed, at the Manchester exposition the chemical equipment firm Buss, of Pratteln, Switzerland, introduced self-contained, skid-mounted, 200-, 500-, and 1,000-L loop reactors especially

Sepracor and Zeneca booths at ChemSpec Europe '94.

for medium-scale hydrogenations.

The Buss name in loop reactors is prestigious, as evidenced by custom producers of fine chemicals who list them by name in their capabilities brochures. Buss units are expensive, however. The new hydrogenation units introduced in Manchester cost $750,000 to buy and about as much to install. SynProTec specializes in designing loop reactor systems around off-the-shelf equipment to keep costs down. How well that approach will compete against Buss remains to be played out.

In a SynProTec system, one reactant is held in a tank and circulates out from the bottom, upward through a static mixer, through a heat exchanger for cooling, through another heat exchanger for heating, and finally back into the top of the tank. The second reactant is added to the first just as the stream leaves the tank and enters the static mixer. The reaction occurs in the mixer and heat exchanger. The one heat exchanger for heating is used only to heat the mixture to the needed temperature.

Hunter says the heat exchanger for cooling can be built to any size needed. Thus heat removal is not the bottleneck, and reactions can be controlled no matter how exothermic. High flow rates increase cooling efficiency, which means that the heat exchanger can be relatively small. The static mixer design favored by SynProTec gives high rates of mass transfer, Hunter says, so reactions of gases or immiscible liquids occur efficiently. Hunter claims that capital costs are low because the tanks, pumps, and heat exchangers are cheaper than jacketed reactors. And he says the concept can be retrofitted to an existing reactor. □

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Solid Sales Gains Finally Kick In For Major Chemical Companies

■ ***Chemical earnings also climb in first quarter as oil, diversified, and pharmaceutical firms post financial gains as well***

William J. Storck,
C&EN Northeast News Bureau

The U.S. chemical industry put in a solid performance in this year's first quarter and, coupled with even better finances the previous quarter, seems to be heading firmly out of the recession.

Although the year-to-year 22% earnings gain in first-quarter 1994 for 30 major chemical companies surveyed by C&EN is less than the 34% rise by these companies in fourth-quarter 1993, the overall results show a more fundamentally sound industry. Perhaps just as important as the healthy earnings gain is the 5% average increase in sales. After essentially three years of almost flat sales in the industry, the news is certainly welcome. And it indicates that, for the first quarter at least, earnings increases are coming from improved business as well as cost cutting.

The improving economy has bolstered downstream domestic markets for chemicals. Rising demand for housing, along with increased purchases of automobiles and other big-ticket durable goods, has led to increased demand for chemicals. As a result, chemical shipments are increasing, inventories are shrinking, and production is up.

According to data from the Commerce Department, the value of shipments of chemicals and allied products in the first quarter grew 3.6% from first-quarter 1993. And for the major subcategory of industrial chemicals, shipments, which for some time had been lackluster at best, rose 2.9%. Meanwhile, inventories of chemicals and allied products fell 2.5% and those of industrial chemicals decreased even more—5.6%.

Whether March, the final month in the quarter, was an aberration or the beginning of a trend remains to be seen, but shipments growth in that month increased strongly, 5.2% from March 1993 for overall chemicals and allied products and 4.4% for industrial chemicals. Although growth in other recent months has slightly exceeded this rate for chemicals and allied products, the increase for industrial chemicals is the highest in almost a year. During March, while inventories of the broader category fell just

Ground rules for C&EN earnings analysis

C&EN's quarterly report on financial performance of the U.S. chemical industry contains data from the 30 largest U.S. basic chemical companies and from 25 oil and diversified companies, each with more than $200 million in annual chemical sales, plus 10 pharmaceutical companies.

To be included in the table of basic chemical producers, a company must have at least 50% of its sales in chemicals. That is why DuPont, for example, is included in the table of diversified manufacturers.

In referring to chemical sales, C&EN means those chemicals whose molecular composition has been changed in the course of manufacture. Hence, chemical sales include those of traditional categories of basic petrochemicals and inorganics, organic intermediates and inorganic compounds, polymers such as plastics and fibers, and agricultural chemicals and specialty derivatives.

Chemical industry leaders for first-quarter 1994

Sales

Rank 1994		$ Millions	Rank 1993
1	Dow Chemical	$4,541.0	1
2	Monsanto	2,001.0	2
3	Union Carbide	1,126.0	3
4	W. R. Grace	1,076.8	4
5	Eastman Chemical	983.0	—
6	Air Products	858.6	5
7	Rohm and Haas	856.0	6
8	Morton International	808.3	9
9	Arco Chemical	757.0	7
10	Hercules	680.0	8

Earnings[a]

	$ Millions	Rank 1993
Monsanto	$194.0	1
Dow Chemical	171.0	2
Air Products	73.1	3
Morton International	71.3	8
Union Carbide	71.0	10
Rohm and Haas	67.0	5
Great Lakes Chemical	66.9	4
International Flavors	58.9	6
Eastman Chemical	56.0	—
Hercules	54.8	9

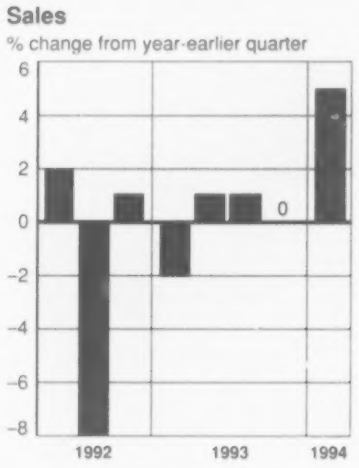
Profitability

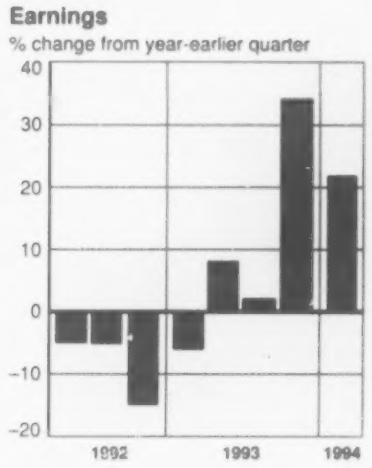
	Earnings as % of sales	Rank 1993
International Flavors	18.2%	1
Great Lakes Chemical	14.9	2
Loctite	11.4	3
Lubrizol	10.9	6
Betz Laboratories	10.7	4
Nalco Chemical	10.1	5
Monsanto	9.7	11
Crompton & Knowles	9.5	7
Morton International	8.8	10
Air Products	8.5	8

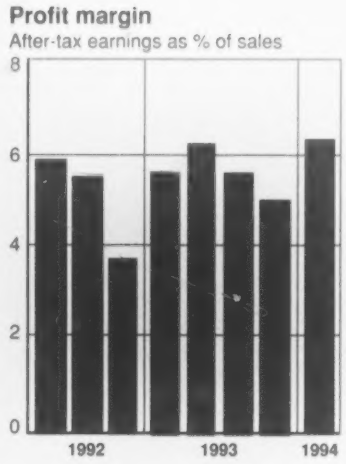
Note: Based on 30 chemical companies listed on page 32. a After taxes.

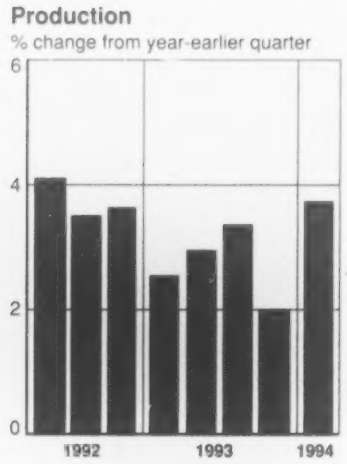
Chemical industry 1994 first-quarter results

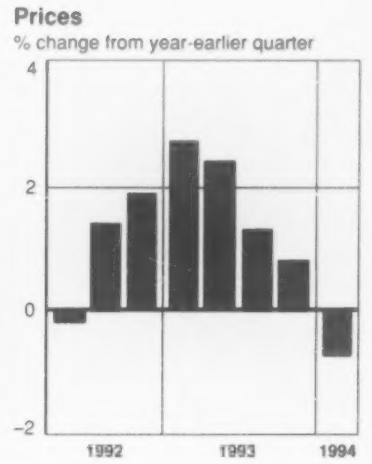
- **Sales increased 5%**
- **Earnings rose 22%**
- **Profitability was 6.4%**
- **Production rose 3.7%**
- **Prices fell almost 1%**











Note: All sales, earnings, and profit-margin data are based on the 30 chemical companies listed on page 32.

2.5%, stocks of industrial chemicals dropped 6.4%.

Production also is increasing to keep pace with the rising demand. For the first quarter, output from chemical plants rose 3.7% on an annual basis. But prices still lag with a first-quarter decline of almost 1.0%.

The result of these factors was that earnings for the 30 chemical companies in first quarter 1994 rose 22% from last year's first quarter to a total $1.27 billion on a 5% sales increase to $19.9 billion. Thus, the aggregate profit margin for the group rose to 6.4% from last year's 5.5%.

The list of the 30 major chemical companies (firms that derive 50% or more of their sales from chemicals) has changed from earlier years because many companies have gone through significant realignments in the past 12 months. Cytec, the chemical spin-off from American Cyanamid, has replaced Cyanamid on the list. Geon, the polyvinyl chloride manufacturer spun off from BF Goodrich, has replaced its former parent. Like Cyanamid, Goodrich has seen its chemical sales shrink below 50% as it concentrates on other business areas. Goodrich has been increasing its aerospace operations; Cyanamid is looking more to drugs for growth.

In addition, Albemarle, the spin-off from Ethyl Corp., has been added to the list, although a much smaller Ethyl remains because now its major business, lubricant and fuel additives, is chemicals. And Eastman Chemical, spun off from Eastman Kodak, has been added to the list. Another change in the list is the shift of Imcera, now called Mallinckrodt Group, to the diversified companies list, because its chemical sales dropped below 50% of its total sales.

The companies that have been added undoubtedly weight the sample more toward chemicals than it has been in years. All of them are essentially 100% chemical companies. Since they replace companies that had large nonchemical

Sales rose for 24 major chemical companies, earnings were up for 22

	FIRST-QUARTER 1994						12-MONTH RUNNING DATA			
	Sales	Earnings[a]	Change from 1993		Profit margin[b]		Change from 1993		Profit margin[b]	
	($ millions)		Sales	Earnings	1994	1993	Sales	Earnings	1994	1993
Air Products	$ 858.6	$ 73.1	3%	-3%	8.5%	9.0%	2%	0%	8.3%	8.4%
Albemarle	241.8	9.8	12	84	4.0	2.5	na	na	na	na
Arco Chemical	757.0	45.0	-1	-13	5.9	6.8	2	-13	6.8	8.0
Betz Laboratories	172.9	18.5	3	-3	10.7	11.4	-1	-14	10.2	11.6
Cabot	434.9	22.3	7	59	5.1	3.4	6	44	4.3	3.2
Crompton & Knowles	133.6	12.8	0	4	9.5	9.2	4	15	9.4	8.5
Cytec	258.1	8.2	10	90	3.2	1.8	na	na	na	na
Dow Chemical	4,541.0	171.0	4	35	3.8	2.9	-2	19	3.5	2.9
Eastman Chemical	983.0	56.0	4	-5	5.7	6.3	3	-8	6.9	7.8
Ethyl	234.0	14.0	-8	-33	6.0	8.3	na	na	na	na
First Mississippi	129.6	4.9	25	nm	3.7	def	6	240	2.2	0.7
H. B. Fuller	242.5	4.0	6	-15	1.7	2.1	5	-15	2.9	3.6
Geon	261.3	7.0	16	nm	2.7	def	11	nm	1.9	def
Georgia Gulf	192.9	12.7	6	26	6.6	5.6	1	6	5.9	5.6
W. R. Grace	1,076.8	38.2	9	21	3.5	3.2	-14	12	5.4	4.1
Great Lakes Chemical	448.7	66.9	4	4	14.9	14.9	15	13	15.1	15.4
Hercules	680.0	54.8	1	22	8.1	6.7	0	31	7.9	6.0
IMC Fertilizer	410.5	5.4	84	nm	1.3	def	37	nm	def	2.7
International Flavors	323.5	58.9	5	5	18.2	18.2	4	5	17.1	17.0
Loctite	159.9	18.3	7	-7	11.4	13.2	2	-18	10.7	13.3
Lubrizol	397.8	43.3	9	22	10.9	9.7	4	10	7.9	7.4
Monsanto	2,001.0	194.0	3	38	9.7	7.3	2	61	6.7	4.3
Morton International	808.3	71.3	25	48	8.8	7.4	21	35	7.7	6.9
Nalco Chemical	336.2	33.8	-1	-4	10.1	10.4	0	3	10.9	10.6
Olin	604.9	15.3	2	31	2.5	2.0	4	-1	1.8	1.9
Petrolite	91.8	5.4	15	12	5.9	6.0	14	28	5.8	5.2
Praxair	611.0	42.0	3	27	6.9	5.6	-4	24	6.4	5.0
Rohm and Haas	856.0	67.0	4	16	7.8	7.0	4	-9	5.8	6.5
Union Carbide	1,126.0	71.0	-6	69	6.3	3.5	-6	88	4.4	2.2
Witco	553.4	22.0	0	17	4.0	3.4	17	38	4.2	3.6
TOTAL	**$19,927.0**	**$1,267.0**	**5%**	**22%**	**6.4%**	**5.5%**	**1%**	**15%**	**5.8%**	**5.2%**

a After-tax earnings from continuing operations, excluding significant nonrecurring and extraordinary items. **b** After-tax earnings as a percentage of sales. **na** = not available. **nm** = not meaningful. **def** = deficit.

operations, chemicals loom larger in the final results of the entire list.

Business was better in the first quarter for most of the 30 companies. Sales were up for 24 of them, and two had the same sales as last year. Additionally, 22 of the 30 companies reported earnings gains, with three—First Mississippi, Geon, and IMC Fertilizer—having posted losses in the first quarter of 1993. Of the 22 companies that did show higher earnings, 16 had double-digit increases—13 of them were greater than 20%.

The largest of these gains was at newly formed Cytec, where earnings improved 90% from what the business units had posted for first-quarter 1993 to $8.2 million on a 10% sales gain to $258 million. Darryl D. Fry, chairman, president, and chief executive officer of the company, says: "Increased sales were reported in substantially all of Cytec's businesses. The strongest gains were in our specialty chemicals businesses due primarily to a strong North American economy, in spite of continued pressure on prices. International sales of specialty chemicals also improved in Europe and Latin America. Our improvement in earnings resulted from increased sales, our continuing emphasis on reducing costs, and higher equity earnings from affiliated companies."

Albemarle, also new, was second highest, with an 84% earnings gain to $9.8 million on a 12% sales increase to $242 million. Floyd D. Gottwald Jr., chairman and CEO, notes: "Our olefins and derivatives business showed a significant improvement in operating results from the prior-year period, especially in poly α-olefins and linear α-olefins. Other favorable areas were flame retardants, polysilicon, and a variety of chemical intermediates. Our first-quarter results are encouraging as we move forward as a new company."

Monsanto posted the largest dollar increase in earnings—$53 million to a total of $194 million. According to chairman and CEO Richard J. Mahoney, "The renewed momentum we had anticipated for our businesses is here. We will continue to fully develop our core products, drive our research investments to commercial success, and find innovative ways to add value for our customers, all

the while keeping an unrelenting pressure on reducing costs."

At Dow Chemical, which also showed a hefty dollar rise of $44 million to a total of $171 million in earnings in the quarter, chairman and CEO Frank Popoff says, "We're very encouraged by the improvement in our operating income, which reflects enhanced productivity, continued economic growth in North America, and the beginning of an upturn in Europe."

The earnings growth was not limited to the chemical companies. A group of 12 oil companies that are major chemical producers reported total earnings up a slight 2% to $2.97 billion on a 5% sales decline to almost $70.0 billion. The aggregate profit margin for the group rose to 4.2% from 4.0%.

Drug companies, of which C&EN surveyed 10, showed slightly better performance, with earnings rising 5% to a total $3.49 billion. Sales rose a much greater 11%, however, to $20.1 billion. This drove the group's profit margin down to 17.4% from 18.4%.

The diversified group of 13 companies that make chemicals showed the biggest gains, with earnings rising an average of 28% to $1.51 billion on just a 3% increase in sales to almost $24.2 billion. Profitability increased to 6.2% from 5.0%.

At DuPont, still the largest U.S. chemical producer but which must be classified as a diversified company because of the huge share of revenues it derives from oil and other nonchemical businesses, earnings increased 39% to $642 million on a slight 1% sales rise to $9.19 billion. Chairman and CEO Edgar S. Woolard Jr. says: "Our significant reduction in costs is having the desired effect on our earnings, but it's also important to note that, compared to last year, we are seeing increased demand in key markets for a number of our businesses, including automotive products, engineering polymers, nylon, Lycra spandex, and nonwovens. Not only is demand generally improved in the U.S., but market conditions are better in Europe and Asia, where our chemicals and specialties sales are up 15% and 6%, respectively."

Although earnings were generally up across the board, chemical executives are not so sanguine as to predict a straight and smooth recovery. On the outlook for his company, but perhaps just as applicable to the U.S. chemical industry, J. Lawrence Wilson, chairman and CEO at Rohm and Haas, says: "We expect volume growth to remain strong as 1994 progresses. We will continue to face an unfavorable currency situation in Europe, but we expect to see additional relief in external economic conditions as the year progresses. And, while selling prices were slightly below last year's level, we did begin to detect a more favorable environment for price increases during the quarter. We will pursue price increases wherever we can. In short, we expect to see continued favorable earnings comparisons as the year unfolds." □

Diversified companies posted strongest earnings gain

	FIRST-QUARTER 1994					
	Sales	Earnings[a]	Change from 1993		Profit margin[b]	
	($ millions)		Sales	Earnings	1994	1993
OIL AND GAS COMPANIES						
Amoco	$ 2,322.0	$ 398.0	–9%	74%	17.1%	8.9%
Ashland	2,206.6	32.9	–8	110	1.5	0.7
Chevron	8,264.0	388.0	–9	–23	4.7	5.5
Exxon	25,964.0	1,160.0	–5	–2	4.5	4.3
Fina	777.5	25.0	–9	30,041	3.2	0
Kerr-McGee	800.9	23.6	2	–3	2.9	3.1
Mobil	15,118.0	535.0	0	9	3.5	3.3
Occidental Petroleum	2,106.0	–34.0	–3	nm	def	3.6
Phillips Petroleum	2,924.0	127.0	–5	108	4.3	2.0
Shell Oil	5,515.0	219.0	–2	15	4.0	3.4
Sun Co.	2,067.0	34.0	–10	–3	1.6	1.5
Unocal	1,916.0	62.0	–17	–37	3.2	4.2
TOTAL	**$69,981.0**	**$2,970.5**	**–5%**	**2%**	**4.2%**	**4.0%**
DIVERSIFIED MANUFACTURERS						
AlliedSignal	$ 2,986.0	$ 169.0	3%	16%	5.7%	5.0%
DuPont	9,190.0	642.0	1	39	7.0	5.1
Engelhard	557.7	22.8	14	43	4.1	3.2
Ferro Corp.	283.3	11.3	10	–14	4.0	5.1
FMC	908.3	46.1	1	2	5.1	5.0
Freeport-McMoRan	449.6	23.4	49	nm	5.2	def
BF Goodrich	502.4	4.9	33	nm	1.0	def
3M	3,632.0	306.0	3	–7	8.4	9.4
Mallinckrodt Group	486.7	42.9	11	41	8.8	6.9
NL Industries	174.2	–6.4	1	nm	def	def
PPG Industries	1,476.9	121.9	2	30	8.3	6.5
Tenneco	3,286.0	129.0	1	74	3.9	2.3
Vulcan Materials	216.9	–5.2	1	nm	def	def
TOTAL	**$24,150.0**	**$1,507.6**	**3%**	**28%**	**6.2%**	**5.0%**
PHARMACEUTICAL COMPANIES						
Abbott Laboratories	$ 2,215.2	$ 366.2	8%	6%	16.5%	16.9%
American Home Products	2,144.0	415.0	2	3	19.4	19.0
Baxter International	2,193.0	131.0	7	8	6.0	5.9
Bristol-Myers Squibb	2,833.9	581.0	3	1	20.5	20.9
Eli Lilly	1,637.0	368.7	5	–1	22.5	23.9
Merck	3,514.3	675.2	48	10	19.2	25.8
Pfizer	1,982.9	370.7	6	6	18.7	18.7
Schering-Plough	1,161.6	253.2	7	13	21.8	20.5
Upjohn	906.0	135.0	–1	–2	14.9	15.1
Warner Lambert	1,472.9	190.4	11	5	12.9	13.6
TOTAL	**$20,060.9**	**$3,486.4**	**11%**	**5%**	**17.4%**	**18.4%**

a After-tax earnings from continuing operations, excluding significant nonrecurring and extraordinary items. b After-tax earnings as a percentage of sales. **nm** = not meaningful. **def** = deficit.